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# All EU hands to the EU pumps: the Science Academies of Europe (EASAC) recommend strong support of research to tackle antibacterial resistance

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## ABSTRACT

Despite many European Union (EU) conferences on fighting microbial resistance, rates of resistance in Europe continue to increase. Although research is catching up with discovery, the development of new antimicrobials is threatened by economic factors, in particular the need for a return of investment via high-volume sales. The EU should invest in independent research into the economic and business aspects of antibiotic development. Multidisciplinary input from the fields of finance, law, marketing, sociology and psychology will inform a broad agenda for change at the regulatory, academic and commercial levels and identify new options for novel anti-infective research and development, as recently recommended by the Science Academies of Europe (EASAC).

**Keywords** antibiotics, drug development, economics, European Union, research

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The European Union's (EU's) attention to the nightmare of antibacterial resistance will soon reach a 10-year mark. While EU conferences succeeded one another after 'the microbial threat' in 1998, rates of resistance to *Neisseria gonorrhoeae* in Europe evolved in parallel with worldwide increases [1], and pandrug-resistant *Acinetobacter baumannii* spread over Europe [2,3]. The EU now has its share of patients for whom the pre-antibiotic era has returned. Meanwhile, in the same period, only a few new antibiotics have been registered. The process of drug discovery and development takes, on average, 10–12 years, and the costs exceed 800 million euro [4].

Why has the global development of new antibiotics been so unsuccessful? Scientific issues such as the difficulty of identifying new classes of antibacterial drugs, or the lack of novel research between 1960 and 2000, are partly responsible, but economic factors are also important. Innovative research is now booming again, both in academic institutions and in small companies [4,5], although Europe is lagging somewhat behind [6]. The major challenge for the near future is not so much discovery, but the development of a safe drug from promising products, which has up to now been a task undertaken by large pharmaceutical companies [3,7,8]. Economic factors are at the heart of the matter. Multinational companies increasingly depend on high-volume sales for return of investment to shareholders, which is contradictory to antibiotic policies [9]. Antimicrobial drugs were banned from the agenda of large companies because of the large number of older off-patent compounds that were negatively influencing drug pricing, a focus on chronic disease and lifestyle drugs in the competition for more secure profits, and finally, the shrinking market as a result of the success of policies restricting the use of new antibiotics. The flow of new drugs, a fundamental societal need or a common good, is driven by financial profit. This constitutes a fundamental moral problem [10]. In addition, high sales undercut the benefit of antibacterial drugs, because high volumes of consumption hasten the development of resistance.

Two EU expert groups have recently recommended to the EU policy-makers that more be invested in research to tackle antibacterial resistance [11,12]. Up to now, the evidence base to guide antibiotic prescribing has been

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astonishingly thin; the diagnosis of infection by culture is slow, and distinguishing bacterial from viral diseases is often difficult in clinical practice. Although the report from the European Technology Assessment Group for Scientific Technology Options Assessment (STOA) includes an interesting analysis of the novel drug development crisis, it recommends research to preserve the older antibiotics, strategies to contain the spread of resistance by improved surveillance and control measures coordinated by the ECDC, the use of rapid diagnostic tests, and efforts to reduce overconsumption and inappropriate use [11]. EASAC experts, representing the science academies of the EU, state that these measures are not sufficient, and plead for research on new drug development with a more rapid and flexible time-scale [12]. Will EU parliamentarians be confused by this apparently contradictory advice? Although both approaches make sense, abandoning investment in new antibacterial drugs will shift shortages to the coming decades.

Europe can learn from the US debate. Some of the incentives for industry proposed by the Infectious Diseases Society of America (IDSA) in the white paper 'Bad bugs no drugs' [13] were recently introduced into legislation concerning bioterrorism after a 'wildcard' proposal was abandoned [8]. Europe is following in the spirit of other actions that have been proposed by the IDSA. The European Commission supports risk capital investment for small and medium-size enterprises in the Competitiveness and Innovation Framework Programme (2007–2013) [14]. The Seventh Framework Programme for Research and Technological Development FP7 will include studies that address the economic burden of resistance [11]. The Innovative Medicines Initiative is one of the two Joint Technology Initiatives, major new elements of FP7. Joint Technology Initiatives, public/private partnerships involving industry (EFPIA), the research community and public authorities, are being set up for the first time at the European level, to pursue ambitious common research objectives [15]. Finally, the scientific committee of the European Medicines Agency (EMEA), responding to the perception that the regulatory process for new drugs has become increasingly stringent, released a think-tank document earlier this year that recommended innovative regulatory approaches and contained specific paragraphs on antibiotics [16].

I would like to launch an EU debate. If we must accept that financial incentives have been driving scientific success in the context of public health in our western societies in the past, Europe should invest in novel independent economic research as a counterpart to the business models that have been unsuccessfully proposed to support industry research and development (R&D) until now. Following the profit problem [17], we need the profit solution. Antibacterial drugs have acquired many characteristics in common with orphan drugs and the drugs used to treat neglected diseases. Concerning the latter, an excellent report, based on an empirical research approach involving reviews of existing knowledge, with recommendations from the London School of Economics and Political Science, is available [9]. Besides such empirical approaches, experimental approaches are needed to gain new insights into the business aspect of novel antibiotic development. Economic research should lead to policies that match appropriate financial incentives to financial motivations. Just as the behavioural sciences are expected to shed light on the driving forces behind antibiotic consumption, there is also scope for multidisciplinary input into EU research to inform a broad agenda for change and to identify new options at the regulatory, academic and commercial levels to support novel anti-infective R&D, as recommended by EASAC. For example, the next step in this endeavour could be the preparation of an EU-funded call for scholarships from EU business schools for PhD programmes concerning financial economics or management research involving a multidisciplinary faculty from the fields of finance, law, marketing, sociology and psychology. An interesting topic for independent research in business ethics would be to consider the motivation beyond corporate social responsibility for antibacterial drug development on the part of drug companies. We need alternative business models for the development of new antibacterial agents, not without the preservation of the older antibiotics. After years of reports and recommendations, it is time for real actions that are paid for with euros, not words. All EU hands to the EU pumps!

## TRANSPARENCY DECLARATION

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